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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/810,262 | 03/26/2004 | Stuart Naylor | 674523-2029.1 | 1123 |

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NEW YORK, NY 10151

| EXAMINER | |
|---|---|
| CHEN, SHIN LIN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1632 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/04/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** 10/810,262 | **Applicant(s)** NAYLOR ET AL. | |
|---|---|---|---|
| | **Examiner** Shin-Lin Chen | **Art Unit** 1632 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 23 April 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1-6,12-14,16-18,47,48 and 50-54*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). 4-23-07
13. ☐ Other: _____.

S Chen

Shin-Lin Chen
Primary Examiner
Art Unit: 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicant argues that Both Balaggan references (2006) teach direct injection into the eye and example 4 of the specification teaches contruction of EIAV-based lentiviral vector comprising polynucleotide encoding various angiostatic genes, such as endostatin and/or angiostatin, under the control of regulatory promoters, such as HRE, CMV promoter and tissue specific promtoer (amendment, p. 5). This is not found persuasive because of the reasons of record. Example 4 only describes prophetic construction of EIAV vectors expressing endostatin and/or angiostatin via either a CMV or HRE promoter, and the use of said vector for in vivo study of age-related macular degeneration. The claims encompass treating retinal or choroidal neovascularization by delivering an EIAV-based lentiviral vector expressing the recited angiogenic gene product under any promoter to the target cells in the eye of a subject via direct injection to target cells. The specification fails to provide adequate guidance and evidence for how to administer an EIAV-based lentiviral vector expressing any angiostatic gene product under any promoter to the target cells in the eye of a subject via direct injection such that sufficient angiostatic gene product can be obtained at the target cells in the eye so as to provide therapeutic effect in vivo for treating retinal or choroidal neovascularization. The specification fails to provide any evidence of what kind of symptom of retinal or choroidal neovascularization has been ameliorated by the treatment. The claims also do not specify what kind of symptom of retinal or choroidal neovascularization has been ameliorated by the treatment. The art of gene therapy in vivo was unpredictable at the time of the invention. Whether sufficient gene product could be obtained at the target cells in the eye with the claimed vector so as to provide therapeutic effect in vivo for treating retinal or choroidal neovascularization was unpredictable at the time of the invention. Further, the biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention. endostatin, angiostatin, VEGFR1, FLT-1 and PEDF have different biological functions. There is no evidence of record that shows that direct injection of EIAV-based lentiviral vector expression those proeins into target cells in the eye would be able to ameliorate symptom of the retinal or choroidal neovascularization. Further, Balaggan et al., 2006 (J. Gene Med.) pseudotyped EIAV vector with VSV-G or rabies-G envelope proteins and said vector express GFP protein rather than any of the angiogenic protein recited in the claim. Therefore, Balaggan et al., 2006 (J. Gene Med.) fails to provide enabling support for the claimed invention. On the other hand, Balaggan et al., 2006 (Gene Therapy) prepare EIAV vector expressing either endostain or angiostatin under the control of CMV promoter and introduce the vector to the eye via subretinal injection. Three weeks after the vector delivery, experimental choroidal neovascularization is induced by using laser, and the endostatin or angiostatin inhibits angiogenesis and vascular hyperpermeability. The EIAV vector was delivered into the eye 3 weeks before the induction of experimental choroidal neovascularization and it appears that this is a prevention experiment rather than a treatment of the CNV. Injection of an EIAV vector into normal eye cells for expression of desired protein is different from injection of EIAV vector into diseased eye cells. There is no evidence of record that shows direct injection of EIAV vector, expressing either endostatin or angiostatin under the control of CMV promoter, into a diseased eye having retinal or choroidal neovascularization would result in sufficient endostatin or angiostatin in the target eye such that therapeutic effect can be obtained and pathological symptoms of retinal or choroidal neovascularization could be ameliorated in vivo. Thus, the Balaggan references fail to provide enabling disclosure for the claimed invention..